

# A Cure is HERE: Overview of Hepatitis C Treatment Landscape

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# Disclosures

Consultant:

Abbvie, Bristol-Myers Squibb, Gilead, Janssen

This talk will include discussion of investigational agents

# Lecture Outline

- Overview and Context
- The past
- The present
- The near future/2016

# Overview and Context

- >3.2 million people in US infected with HCV
  - Many (~50%) unaware of diagnosis
- #1 indication for liver transplant in US
- Associated with rise in hepatocellular carcinoma
- Majority are genotype 1
- We believe HCV can be cured
  - Unlike HIV or HBV
- 6 new drugs/combinations approved in last 4 years
- 3 new drugs pending FDA approval currently

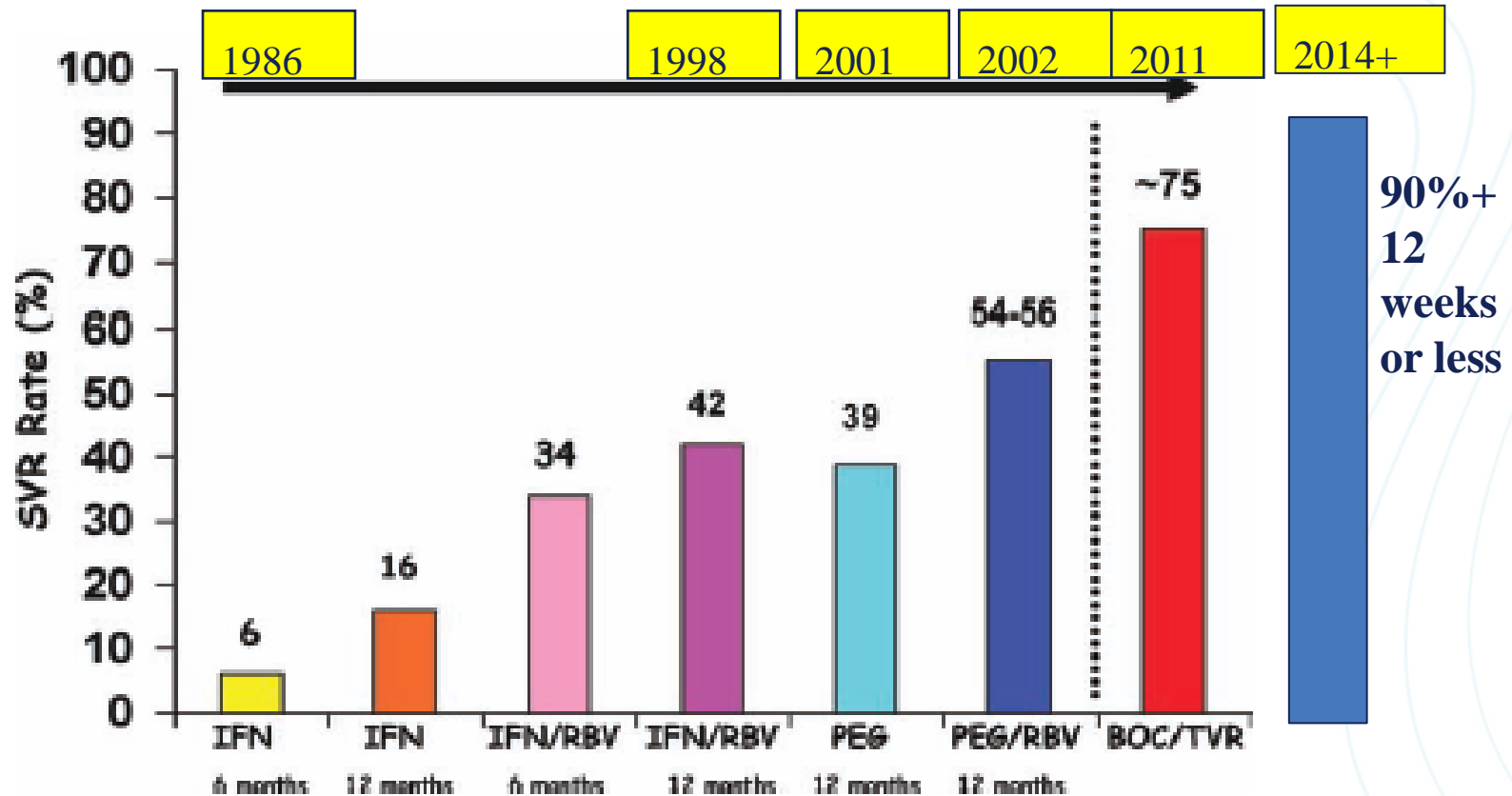
# Overview and Context

- Majority of patients infected will develop chronic infection (80%)
- 20-50% will progress to cirrhosis ± HCC
  - Over 15-30 years
- Risk factors for progression
  - Concurrent EtOH, HIV coinfection, male, age >40 at acquisition, longer duration of disease
- Sustained virologic response (SVR) = goal of Rx
- Feeling more comfortable saying SVR24 = “cure”

# PA-Centric Overview and Context

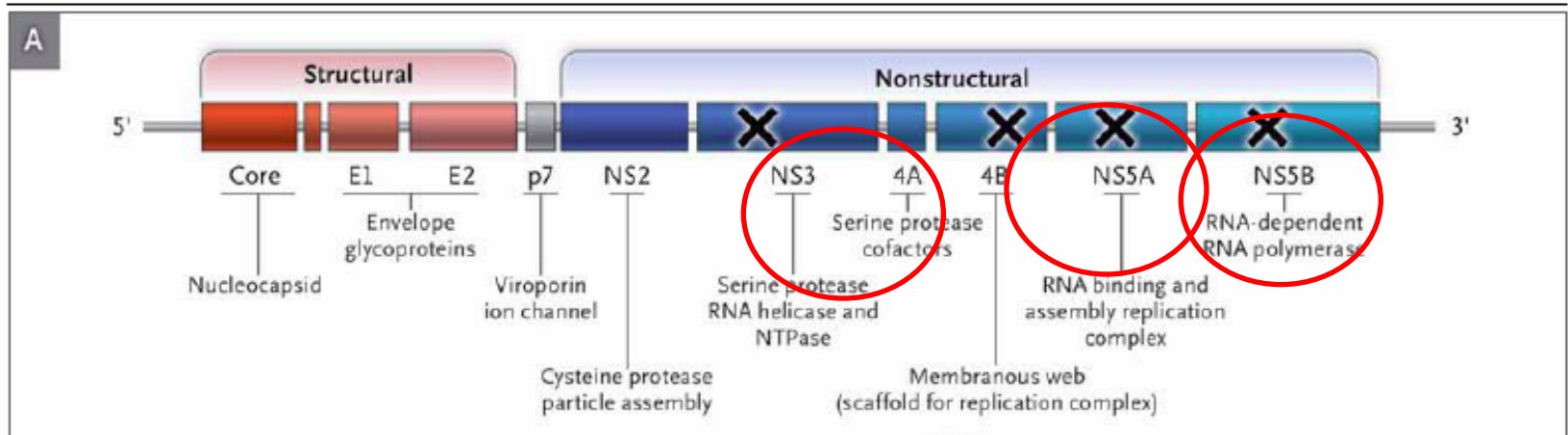
- >150,000 Pennsylvanians infected with HCV
- >45,000 Philadelphians infected with HCV
- 18.1% prevalence of anti-HCV in PA state prison system
  - 53% of infection younger than CDC birth cohort

# Historical HCV Treatment



# Brief Pathophysiology of Rx

- Standard” HCV treatment causes an anti-viral state within the host cell → viral eradication
  - Many side effects
  - Does not directly act against HCV itself
- HCV genome composed of  $\geq 10$  polyproteins with direct roles in virus life cycle





# The Past: 2001-2011



OR



48  
weeks

# The Past: 2011-2013



OR



OR



24-48  
weeks

# The Past: 2013-2014



OR



OR



12-24 weeks

# 2014 - present



OR



OR



**viekira pak™**  
ombitasvir, paritaprevir and  
ritonavir tablets; dasabuvir tablets

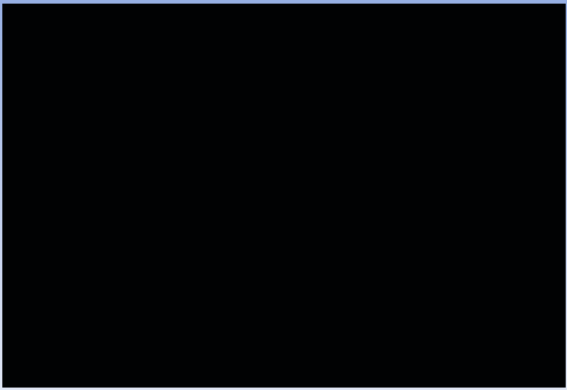


8-24  
weeks

# Hepatitis C Rx - The Present

- Need to know HCV genotype & cirrhosis status ( $\pm$ )
  - For g1: ledipasvir/sofosbuvir; sofosbuvir + simeprevir; paritaprevir/r/ombitasvir/dasabuvir
  - For g2/3: sofosbuvir + ribavirin
  - For g4: Peg-interferon + ribavirin + sofosbuvir; sofosbuvir + ribavirin;
  - Treatment ranges from 8-24 weeks
- Interferon-free option now available for g1-4
- [www.hcvguidelines.org](http://www.hcvguidelines.org) = rapid guidelines site
  - Joint effort between AASLD and IDSA

# Hepatitis C - Approved at Present

Protease Inhibitors	Polymerase Inhibitors	NS5A inhibitors
	Sofosbuvir (Sovaldi) (g1-4, 1 tab daily)	Ledipasvir/Sofosbuvir (Harvoni) g1 1 tab daily
	Simeprevir (Olysio) (g1, 1 cap daily)	
	Paritaprevir/ritonavir/Ombitasvir + Dasabuvir (Viekira-Pak) g1, 3 tabs in AM, 1 in PM	

# Mnemonic to remember DAA's

- Look at end of the drug's name
  - PREvir = PRotEase inhibitor
    - eg. Telaprevir, boceprevir, simeprevir
  - Uvir = nUcleotide or non-nUcleotide polymerase inhibitor
    - eg. Sofosbuvir, dasabuvir
  - Asvir = NS5A inhibitor
    - eg. Ledipasvir, ombitasvir, daclatasvir,

This works so far...

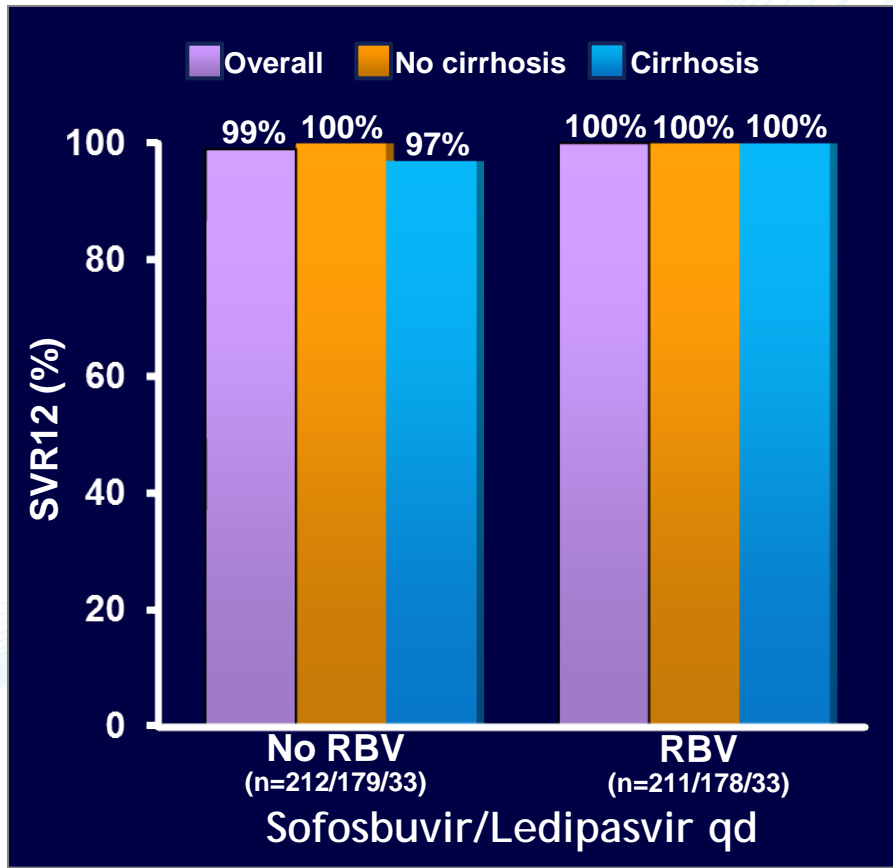
# FDA-approved all-oral options g1

- **Ledipasvir/Sofosbuvir 90mg/400mg**
  - 1 tab daily x 12 weeks for most patients
  - 24 weeks if treatment-experienced and cirrhotic
  - Consider 8 weeks if HCV RNA < 6 million IU/mL and no cirrhosis
- **Simeprevir 150mg + Sofosbuvir 400mg**
  - 2 pills once daily (1 of each)
  - 12 weeks if no cirrhosis
  - 24 weeks if cirrhosis present
- **Paritaprevir/r/ombitasvir+dasabuvir (75/50/12.5+250mg)**
  - 3 tabs in AM + 1 tab in PM
  - Without ribavirin for g1b without cirrhosis
  - With ribavirin for g1a ± cirrhosis or g1b + cirrhosis
  - 12 weeks except 24 weeks if g1a cirrhosis



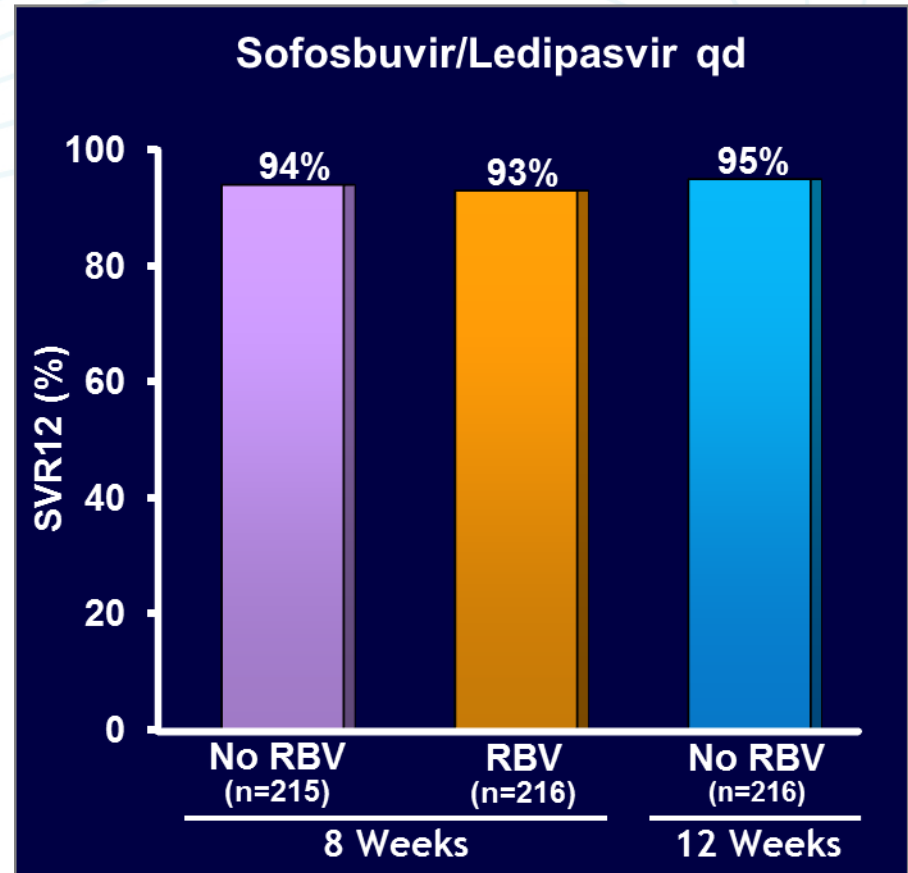
# ION-1: SVR12 Rates With Sofosbuvir/Ledipasvir $\pm$ RBV Treatment-Naïve, HCV G1

## 12-Week Arm



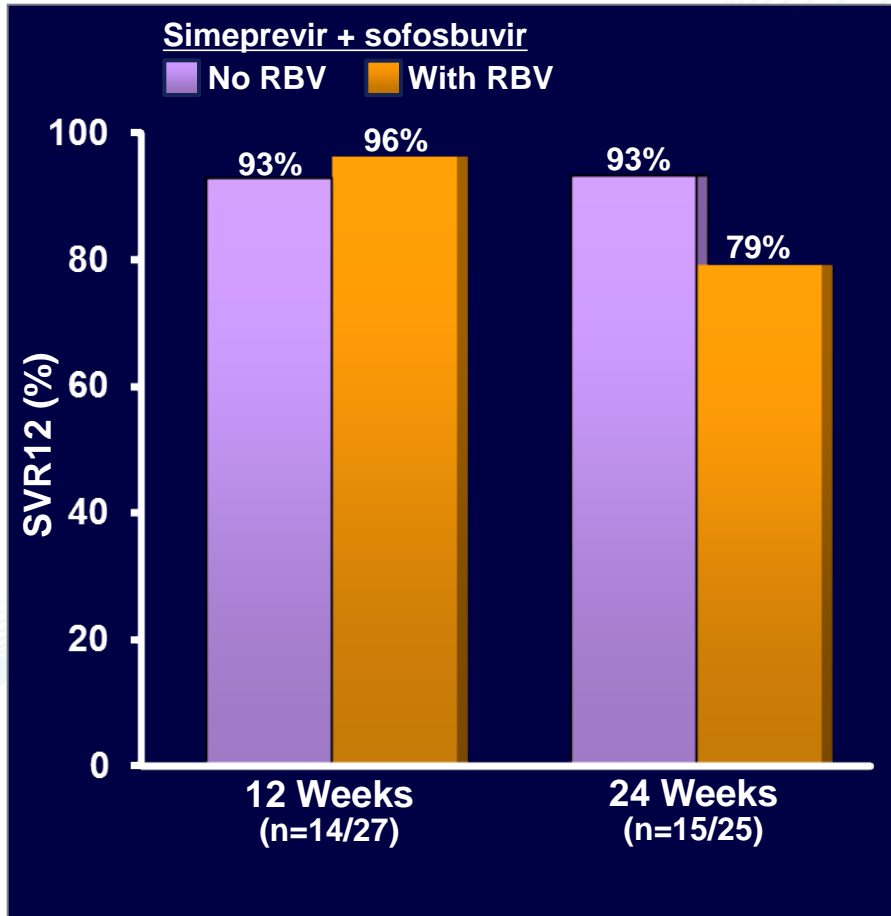
# ION-3: SVR12 Rates W/ SOF/LDV $\pm$ RBV in Treatment-Naïve, HCV G1

## Overall SVR12\*

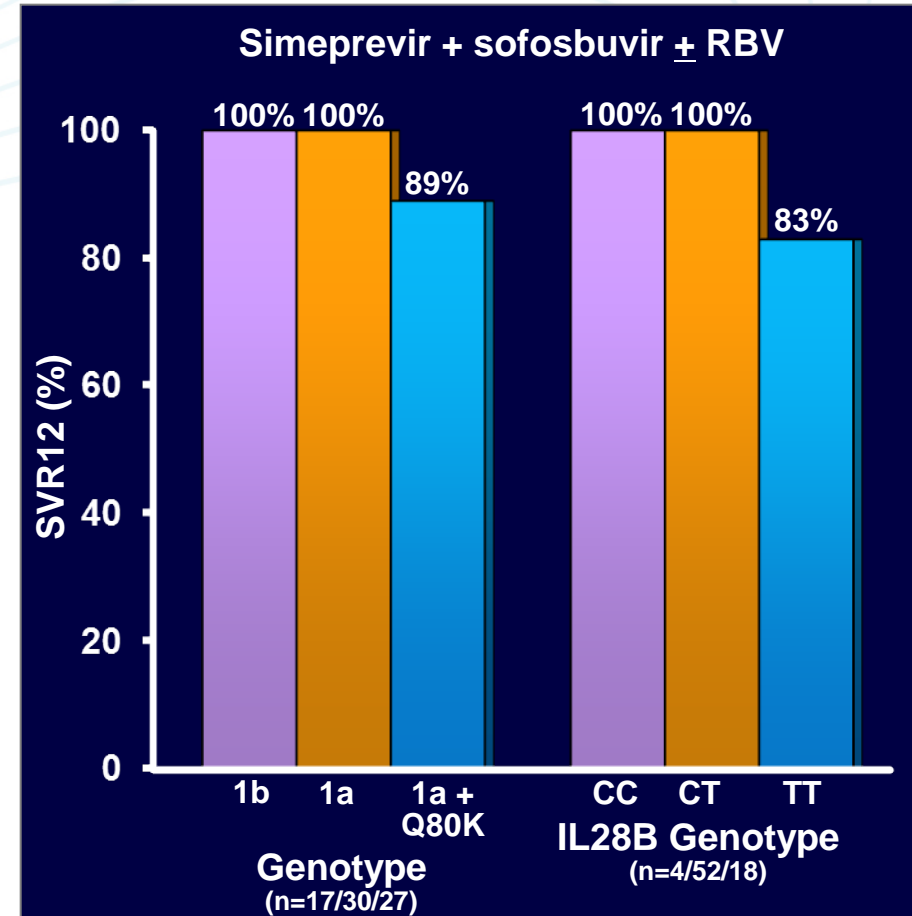


# COSMOS Subgroup Analysis: SVR12 in Genotype 1 Prior Null Responders (F0-F2)

## SVR12



## SVR12 by HCV Subtype



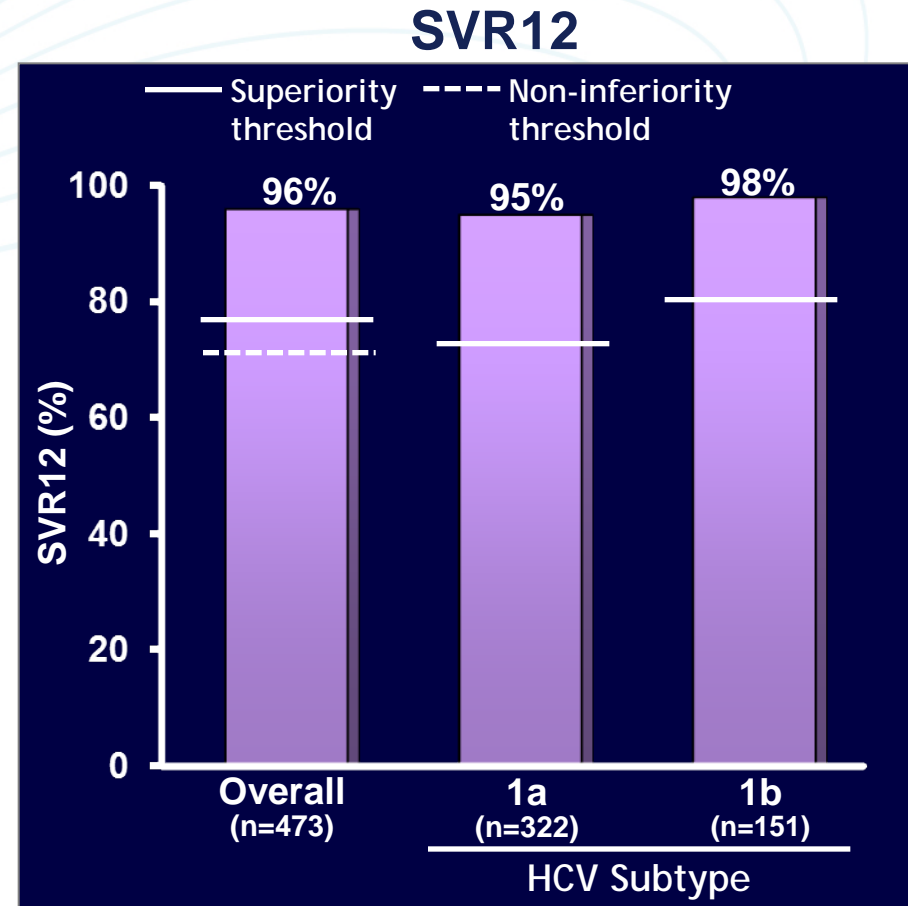
Lawitz E, et al. Lancet 2014; ePub July 28, 2014.

Sulkowski MS, et al. J Hepatol. 2014;60(suppl 1):S4. Abstract O7.

# SAPPHIRE-I: SVR12 Rates With 3D + RBV in Treatment-Naïve, HCV Genotype 1



- Non-inferiority and superiority criteria met for overall SVR12 and superiority criteria met for SVR rate for genotype 1a and 1b
- SVR12 rates were similar across patient subgroups
- SVR12 non-achievers
  - Virologic breakthrough (n=1)
  - Relapse (n=7)
    - Genotype 1a
  - All had  $\geq 1$  RAV at time of virologic failure



# FDA-approved options

- **Genotype 2 -**

- Sofosbuvir 400mg 1 tab PO daily + weight-based ribavirin PO x 12 weeks
- Peg-interferon alfa 2a/2b subcut weekly + ribavirin 400mg PO BID x 24 weeks

- **Genotype 3 -**

- Sofosbuvir 400mg 1 tab PO daily + weight-based ribavirin PO x 24 weeks
- Peg-interferon alfa 2a/2b subcut weekly + ribavirin 400mg PO BID x 24 weeks

# Side Effects of New Meds

- Infrequent (<20%) and minor
- Headache, nausea, fatigue, insomnia
  - Patient reaction #1: “I already have all of those”
  - Patient reaction #2: “Do I really have to come in and pay my copay? I feel so good!”
- “InterFEARon” era is over
- Patients and providers won’t accept interferon-based Rx
- Management MUCH easier now
  
- Pre-2013: Side effects → treatment avoidance
- Post-2013: Access → treatment avoidance

# Who should be treated?

- Everyone
- So why aren't they?
  - Cost
  - Insurance requirements
  - Access to providers
  - Underdiagnosis
  - Linkage to care
  - Number of providers?

# Who Do I Treat Now?

- **Highest Priority for Treatment Owing to Highest Risk for Severe Complications**
  - Advanced fibrosis (F3)/compensated cirrhosis (F4) (Class I, Level A)
  - Organ transplant (Class I, Level B)
  - Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis) (Class I, Level B)
  - Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis (Class IIa, Level B)
- **High Priority for Treatment Owing to High Risk for Complications**
  - Fibrosis (Metavir F2) (Class I, level B)
  - HIV-1 coinfection (Class I, Level B)
  - HBV coinfection (Class IIa, Level C)
  - Other coexistent liver disease (eg, NASH) (Class IIa, Level C)
  - Debilitating fatigue (Class IIa, Level B)
  - Type 2 Diabetes mellitus (insulin resistant) (Class IIa, Level B)
  - Porphyria cutanea tarda (Class IIb, Level C)

# Who Do I Treat Now?

- **Persons Whose Risk of HCV Transmission is High and in Whom HCV Treatment May Yield Transmission Reduction Benefits**
  - MSM with high-risk sexual practices
  - Active injection drug users
  - Incarcerated persons
  - Persons on long-term hemodialysis
    - Rating: Class IIa, Level C
  - \*Patients at high risk of transmitting HCV should be counseled on ways to decrease transmission and minimize the risk of reinfection.



# Hepatitis C - The Future

<b>Protease Inhibitors</b>	<b>Polymerase Inhibitors</b>	<b>NS5A Inhibitors</b>
<b>grazoprevir</b>	ACH-3422	<b>elbasvir</b>
sovaprevir	MK-3682	<b>daclatasvir</b>
ABT-493	BMS-791325	GS-5816
vedroprevir	ALS-2200	ABT-530
		ACH-3102

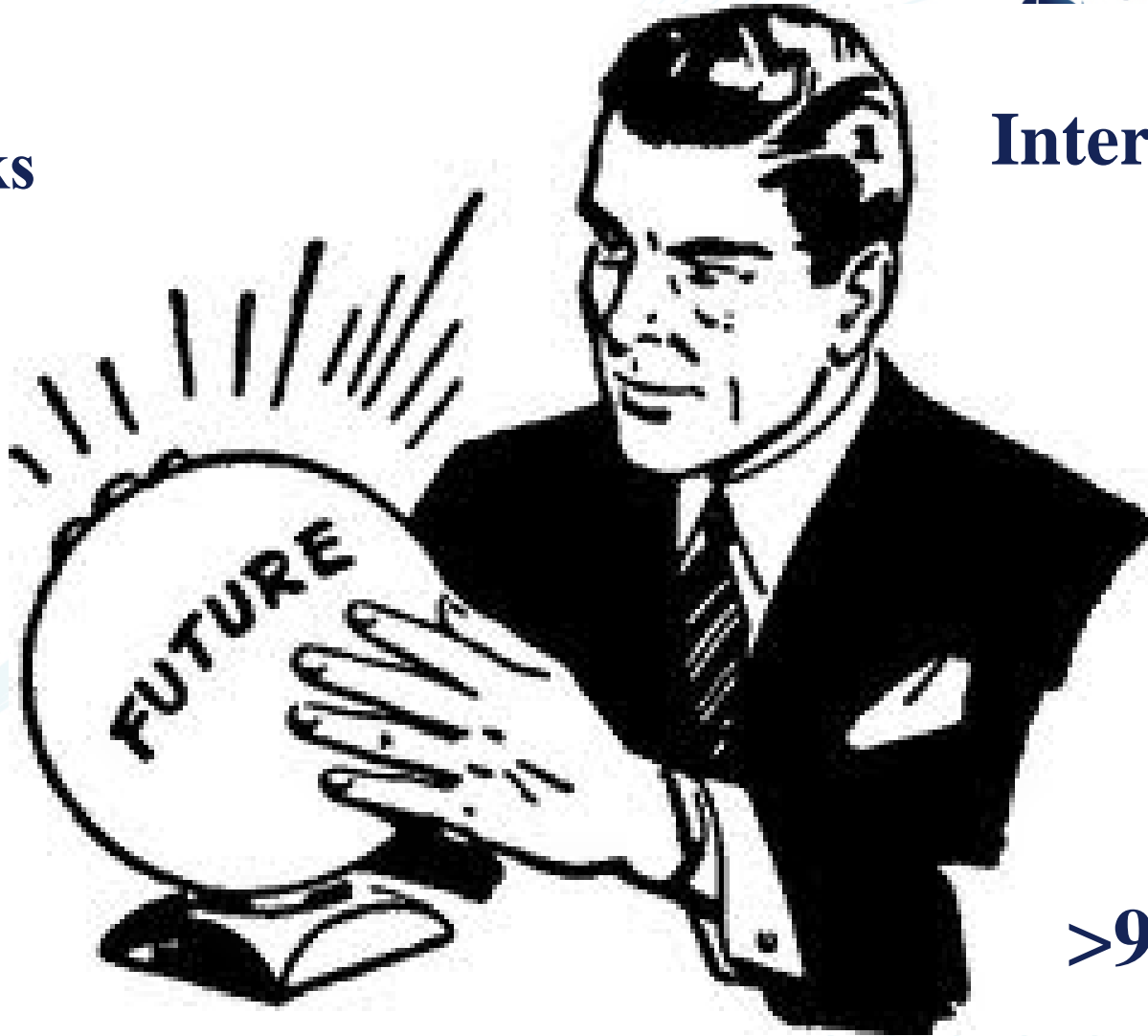
+ many more individual agents and combinations...

**≤12 weeks**

**Interferon-free**

**All-oral**

**One pill**



**>95% SVR**

**UNIVERSAL ACCESS**

# Conclusions

- SVR rates now are >90% for many patients
- Treatment landscape is expected to rapidly change over next few years
- The days of interferon are gone
- Pricing/competition/insurers (aka ACCESS) likely to be biggest hurdle in next few years as efficacy will be >95% for most combinations and patients
- Remember [hcvguidelines.org](http://hcvguidelines.org)

# Contact Information



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# Understanding Hepatitis C Treatment Access

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Clinical Professor of Law &  
Director, Center for Health Law and Policy Innovation of Harvard Law School

May 2015

# Comments Based on Findings of Recently Released Report

## EXAMINING HEPATITIS C VIRUS TREATMENT ACCESS



### A REVIEW OF SELECT STATE MEDICAID FEE-FOR-SERVICE AND MANAGED CARE PROGRAMS

- Examines accessibility of Sovaldi through Medicaid fee-for-service in 10 states
- Also examines Sovaldi access in 5 select states Medicaid managed care plans
- Report and corresponding webinar available at [www.chlpi.org](http://www.chlpi.org)

# Limitations on Access to HCV Treatments

- **Limits Based on Stage of Fibrosis**
- **Restrictions Based on Substance Use**
- **Prescriber Limitations**
- **Other restrictions**
  - HIV Co-Infection limitations
  - “Once per lifetime” limitations
  - Genotype limitations
  - Previous history of treatment adherence requirements
  - Specialty pharmacy restrictions
  - Exclusivity agreements with insurers

# Illinois Sovaldi Prior Authorization Criteria: More Restrictive Than Most States

## Coverage

- + Non-preferred drug

## Fibrosis

- + Metavir score of  $\geq F4$

## Substance Use

- + No evidence of substance abuse in past 12 months

## Prescriber Limitations

- + If prescriber is not a specialist, required one-time written consultation within past 3 months



# MassHealth FFS Sovaldi Prior Authorization Criteria: Less Restrictive Than Most States

## **Coverage**

- + Preferred drug

## **Fibrosis**

- + No restrictions (form inquires)

## **Substance Use**

- + No restrictions (form inquires about current use)

## **Prescriber Limitations**

- + No restrictions

## **Additional Restrictions**

- + No additional restrictions based on HIV Co-infection or previous adherence

# MassHealth MCOs Sovaldi Prior Authorization Criteria

	<b>Boston Med. Ctr. Health Net Plan</b>	<b>Neighborhood Health Plan</b>	<b>Tufts Health Plan Network Health</b>	<b>Health New England</b>
<b>Fibrosis</b>	F3-4	F3-4	F3-4	F4
<b>Requirements Related to Substance Use</b>	Not abused substances for 6 months	(For members with past/current issues) abstain from use for 6 months and participation in supportive care	No substance abuse within past 6 months OR receiving counseling services	(Known substance abusers) must have been referred to specialist; abstinence from substance abuse for 6 months; ongoing participation in treatment program; adequate psychosocial supports
<b>Prescriber Limitations</b>	Prescribed by or in consultation with specialist	Prescribed by or in consultation with specialist	Prescribed by specialist	Prescribed by specialist
<b>HIV Co-Infection</b>	Yes, with non- suppressable viral load or elevated MELD scores	Not without meeting additional requirements above	Not without meeting additional requirements above	Yes, if compliant with antiretroviral therapy as indicated by undetectable viral load
<b>Additional Adherence Requirements</b>	No history of nonadherence; enrollment in compliance monitoring program	Individual must demonstrate understanding of the proposed treatment, and display the ability to adhere to clinical appointments	"[M]ember has been assessed for potential nonadherence."	No ongoing non-adherence to previously scheduled appointments, meds or treatment; adherence counseling; willing to commit to monitoring

# Massachusetts Affordable Care Act Qualified Health Plans – Prior Authorization Criteria

	Fallon Health	Tufts	Harvard Pilgrim
<b>Fibrosis</b>	<b>F3-4</b>	<b>F3-4</b>	<b>F3-4</b>
<b>Requirements Related to Substance Use</b>	"[N]ot engaged in any habits that would negate the efficacy of the medications."	No illicit substance abuse within past 6 months OR receiving substance or alcohol abuse counselling services/seeing addiction specialist	None
<b>Prescriber Limitations</b>	Prescribed by specialist	Prescribed by specialist	Prescribed or supervised by specialist
<b>HIV Co-Infection</b>	None. Must meet other criteria as listed on this chart.	None. Must meet other criteria as listed on this chart.	None. Must meet other criteria as listed on this chart.
<b>Additional Adherence Requirements</b>	Must have been adherent to past therapies; must be prepared/motivated to start treatment. Application "require[s] a member's psychological and behavioral habits assessment to determine if therapy is right for him/her."	"[M]ember has been assessed for potential nonadherence."	None

# Pennsylvania FFS Sovaldi Prior Authorization Criteria

## Coverage

- + Preferred drug

## Fibrosis

- + Metavir score of  $\geq$ F3-4

## Substance Use

- + “Documented history” of abstinence from alcohol/drugs for at least 6 months
- + Individuals with history of substance dependence must also have a lab test that supports abstinence and comply with any treatment

## Prescriber Limitations

- + Prescriber must be a specialist

## Additional Restrictions

- + No severe renal impairment or end stage renal disease

# Pennsylvania MCOs Sovaldi Prior Authorization Criteria

	<b>UPMC Health Plan (PA form only)</b>	<b>United Healthcare Community &amp; State</b>	<b>Aetna Better Health</b>	<b>Gateway Health (non-formulary)</b>
<b>Fibrosis</b>	Asks if patient has advanced fibrosis or decompensated cirrhosis	F3-4	F3-4 or F2 with serious extra-hepatic manifestations of HCV	F3-4
<b>Requirements Related to Substance Use</b>	(Known substance abusers) must provide documentation of: abstinence from drugs for 3 months; urine drug screen within past 3 months; and that member has been screened for alcohol abuse	If there is a known history of illicit drug or alcohol abuse, must have abstained from abuse for past 6 months AND submit negative urine drug screen collected within 30 days of onset of treatment	Requires documentation to support abstinence from alcohol or illicit drugs for at least 6 months as well as compliance with dependency treatment	No diagnosis of alcohol or substance abuse, or documented history of abstinence for at least 12 months prior to treatment, including adherence to any prescribed substance abuse treatment and pertinent lab testing
<b>Prescriber Limitations</b>	Not specified	Prescribed by a specialist	Prescribed by or in consultation with a specialist	Prescribed by specialist
<b>HIV Co-Infection</b>	N/A	Appears that individuals who are co-infected with HIV do not have to meet fibrosis criteria	N/A	Plan states that individuals with HIV who meet applicable criteria are eligible
<b>Additional Adherence Requirements</b>	N/A	N/A	Documentation of treatment compliance and adherence counseling	Individual must commit in writing to a treatment agreement

# Pennsylvania Affordable Care Act Qualified Health Plans – Prior Authorization Criteria

	Blue Cross of Northeastern Pennsylvania	Independence Blue Cross	UPMC Health Plan
<b>Fibrosis</b>	F3-4	Inquires about fibrosis score	Inquires about fibrosis score
<b>Requirements Related to Substance Use</b>	N/A	N/A	Inquires about history of substance abuse
<b>Prescriber Limitations</b>	Prescribed by specialist	N/A	Inquires about provider specialty

## Other QHPs:

**Aetna:** not covered

**Assurant Health:** covered; PA information only available by calling # on member ID card

**Capital BlueCross:** covered; PA directed to CVS (general form)

**Geisinger Health Plans:** not covered

**Highmark Health Insurance Company:** covered ; PA criteria unavailable

**UnitedHealthcare:** information unavailable

## NEXT STEPS

### Reframe the Response

#### Shift the focus from cost to cure

- + Recognize payor concerns, but accurately assess the value of cure
- + With supplemental rebates the cure is now ~\$40,000
- + Comparative effectiveness matters
  - + We paid over ~\$250,000 per HCV cure in interferon age
  - + In HIV, no cure and we pay ~\$10,000 per year for life for HAART
- + Pharmacy budgets may increase but others will decrease
- + U.S. government sets pharma laws with varying perspectives if effective – If not, change laws, rather than deny access to HCV cure
- + Medicaid is an entitlement program in part to grow to meet the demands created by innovation

# Respond to HCV Treatment Advances From a Public Health Perspective

## HCV must be addressed as a serious public health issue

- + Screening and treatment have significant individual and public health benefits
- + Baby boomer generation is not the end of the epidemic, with increasing evidence of growing incidence in young people
- + Other serious diseases are not similarly treated (i.e., requiring disease progression or sobriety) and this undermines the public health response
- + Insurers should adopt, not ignore, lessons learned from HIV treatment guidelines, where early and unrestricted access is the rule



## Follow Medicaid and ACA Law

### **Both public and private health insurance laws preclude restrictive, unfair and discriminatory HCV treatment access practices**

- Under the Medicaid Act all prescription drugs of a manufacturer who enters into rebate agreements must be covered, with only exceptions allowed for safety and clinical effectiveness
- While states have more discretion under prior authorization, even here courts have supported challenges when access is severely curtailed or final authority to provide drugs does not rest with the prescribing health care providers
- Under Massachusetts law, as well as in other states, state medical necessity laws require even fewer restrictions on access to effective, life-saving medications
- Under the ACA differential treatment of HCV rises to the level of a discriminatory insurance practice

# Advocate for Broader Access for Many People Living with HCV By Securing Adequate Medicaid Coverage

## State Medicaid Expansion

- + 29 states (including DC) adopted the Medicaid expansion; under discussion in 6 states; 16 states are not adopting<sup>10</sup>

## Pharmacy and Therapeutics Committees

- + Providers, clinicians, and other partners make up the committee
- + Decide which drugs are included on formularies and what prior authorization criteria are attached to each drug

## Fee-for-Service (FFS) vs. Managed Care Organizations (MCOs)

- + Most of the Medicaid population is shifting to MCOs<sup>11</sup>
- + Some MCOs follow the state FFS guidelines, others set own criteria